REMARKS

The application has been rejected under 35 USC §112, first and second paragraphs and 35 USC §102(a) and (b).

§112, First Paragraph

The Examiner rejected claims 12 and 13 stating that while the specification is enabling for competitive receptor binding assays for certain compounds using the compounds of claims 1 and 3, the specification does not provided enablement for the analogous use of all of the compounds of claim 6. The Examiner states that the specification does not enable any person skilled in the art to use the invention commensurate in scope with the claims. For instance, the Examiner states that it is unclear how the method would work for the cases in which the compounds of claim 6 are very closely related to the pharmaceutical.

Applications respectfully disagree with the Examiner's conclusion. The test for enablement is whether one skilled in the art could make or use the invention with reference to the disclosure itself and what was known in the art without undue experimentation. See MPEP 2164.01. While experimentation may be necessary, such experimentation is not undue. For instance, many of the compounds are known. See Specification page 2, **[0003]** and page 5, **[0012]** citing US 5,665,727. The experiments to determine whether or not a particular compound would work are straightforward and well within the realm of one of ordinary skill in the art. The breadth of the claim makes it clear which compounds fit within the scope of the claims. As to the Examiner's specific example, it is clear that one skilled in the art would merely determine the binding of the competitor to the receptor in comparison with the pharmaceutical. This work is routine and there is clear guidance in the claims and the specification. See MPEP 2164.01(a) and *In re Wands*, 858 F.2d 731.

Thus, Applicants respectfully request that the rejection be withdrawn.

§112, Second Paragraph

Claims 2, 4, and 6-13 are rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 4 have been cancelled so the rejections are moot to these claims. It is believed that the amendments to claims 6, 7, 9, 12 overcome the rejections as to parts 5(a) to (g) of the Examiner's response. Applicants thank the Examiner for the helpful suggestions.

With reference to claims 7, 9 and 12 and the rejection in part 5(h) the Examiner states that the steps which effect "detecting" and "correlating" are incomplete. Applicants respectfully traverse the rejection. The claim is reasonable definite to one of ordinary skill in the art. Recent cases in the **United States Court of Appeals for the Federal Circuit** have confirmed validity of claims with very similar terms. See, METABOLITE LABORATORIES, INC. and COMPETITIVE TECHNOLOGIES, INC., Plaintiffs-Appellees, v. LABORATORY CORPORATION OF AMERICA HOLDINGS (doing business as LabCorp), Defendant-Appellant at 370 F.3d 1354. (Fed. Cir. 2004) The patent at issue was U.S. Patent No. 4,940,658. Claim 13 reads:

13. A method for detecting a deficiency of cobalamin or folate in warm-blooded animals comprising the steps of: assaying a body fluid for an elevated level of total homocysteine; and correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate.

Further MPEP 2173.02 referring to *Metabolite* states: "The requirement to "distinctly" claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles ...". The claims meet the requirements of §112, seconfd paragraph and are not vague or indefinite. Thus, Applicants respectfully request that the rejection be withdrawn.

§102 (a) and (b)

The Examiner has rejected Claims 1-6 as being anticipated by each of Fujisawa (WO/92/00313) and Kobayashi et al (US 6,338,946) under 102(a) and by Fujisawa (WO 91/17754) under 102(b). Further Claim 6 has been rejected under 102(b) as being anticipated by Fujisawa (WO 91/02736) and US 5,665,727. Claims 1-5 have been cancelled. Thus, the rejection is moot to those claims.

With reference to Claim 6, the Examiner states that, while giving no weight to an intended method of use in a product claim, the compound appears to be the same as Claim 3 of Kabyashi et. al and are anticipated by 91/02736, formula (I) and the '727 formula (I). Applicants traverse. As stated in *Metabolite,* "A preamble may provide context for claim construction, particularly, where as here, that preamble's statement of intended use forms the basis for distinguishing the prior art in the patent's prosecution history. Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 809 (Fed. Cir. 2002) (in rare circumstances, a preamble's recitation of intended use may serve to distinguish the prior art)." Moreover, Applicants believe the amendments to claim 6 further distinguish the claim from the references. The references do not disclose or suggest an assay reagent as claimed.

Thus, Applicants submit that the claims as amended are not anticipated by the references and respectfully request that the rejection be withdrawn.

Applicants submit that the amendments and remarks overcome the Examiner's rejections. The Examiner is encouraged to contact the undersigned if the Examiner has any matter that she would like to address.

Respectfully submitted,

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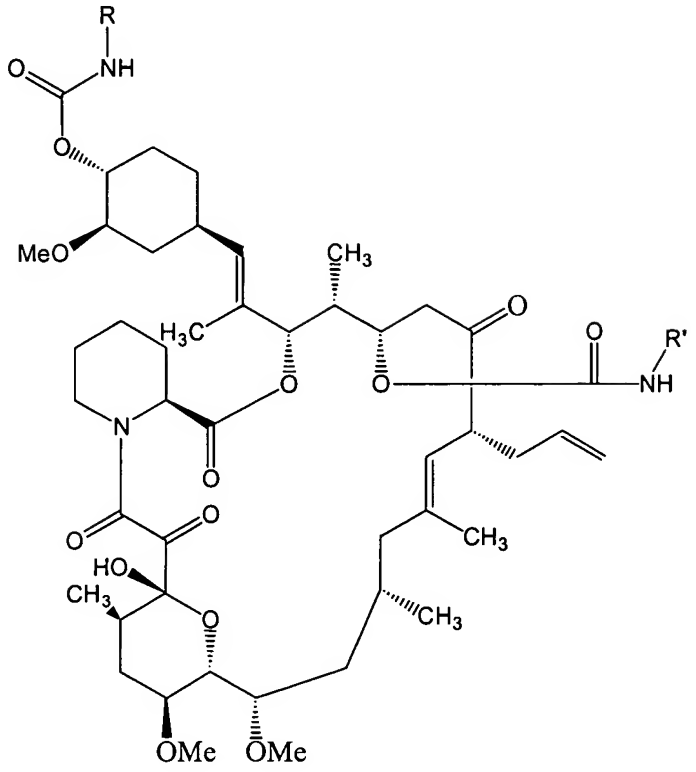
CLAIMS (CLEAN COPY)

Claim 1 (canceled).



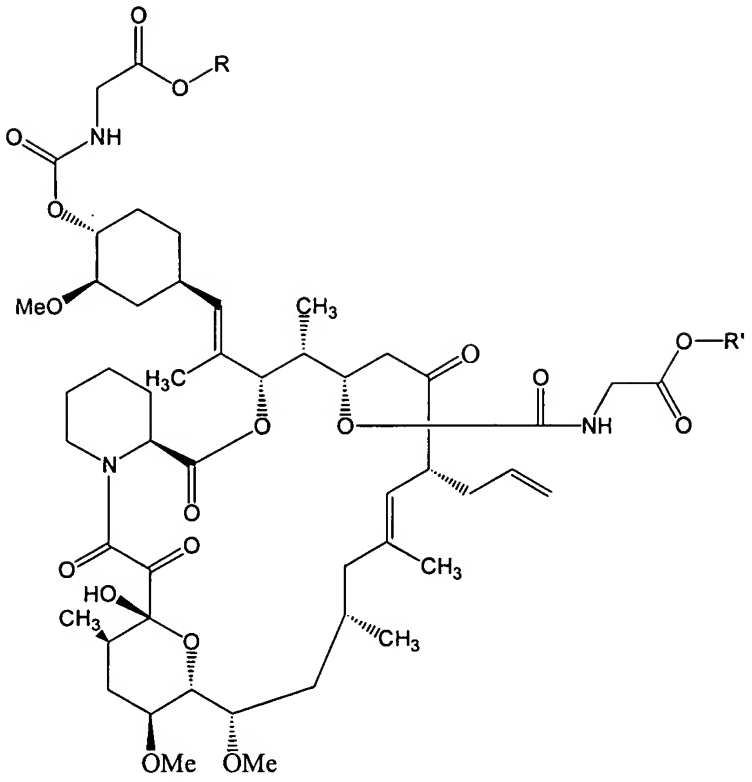
or solvate thereof, wherein

R is alkyl, aryl, allyl, each having less than 25 carbons or H, and

R' is alkyl, aryl, allyl, each having less than 25 carbons or H.

2 (canceled) The compound of claim 1 wherein R or R' further comprise at least one functional group selected from the group consisting of esters, ethers, amides, phosphates, sulfonates, sulfate, amidines, phosphonates, or carboxylate functional groups.

3 (canceled) A compound having the formula:



or solvate thereof, wherein

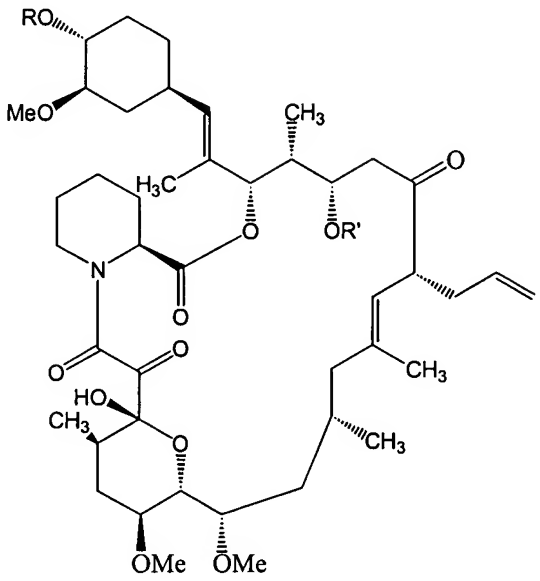
R is alkyl, aryl, allyl, each having less than 25 carbons or H, and

R' is alkyl, aryl, allyl, each having less than 25 carbons or H.

4 (canceled) The compound of claim 3 wherein R or R' further comprise at least one functional group selected from the group consisting of esters, ethers, amides, phosphates, sulfonates, sulfate, amidines, phosphonates, amine, hydroxyl, or carboxylate functional groups.

5 (canceled) The compound of claim 3 wherein R or R' is ethyl.

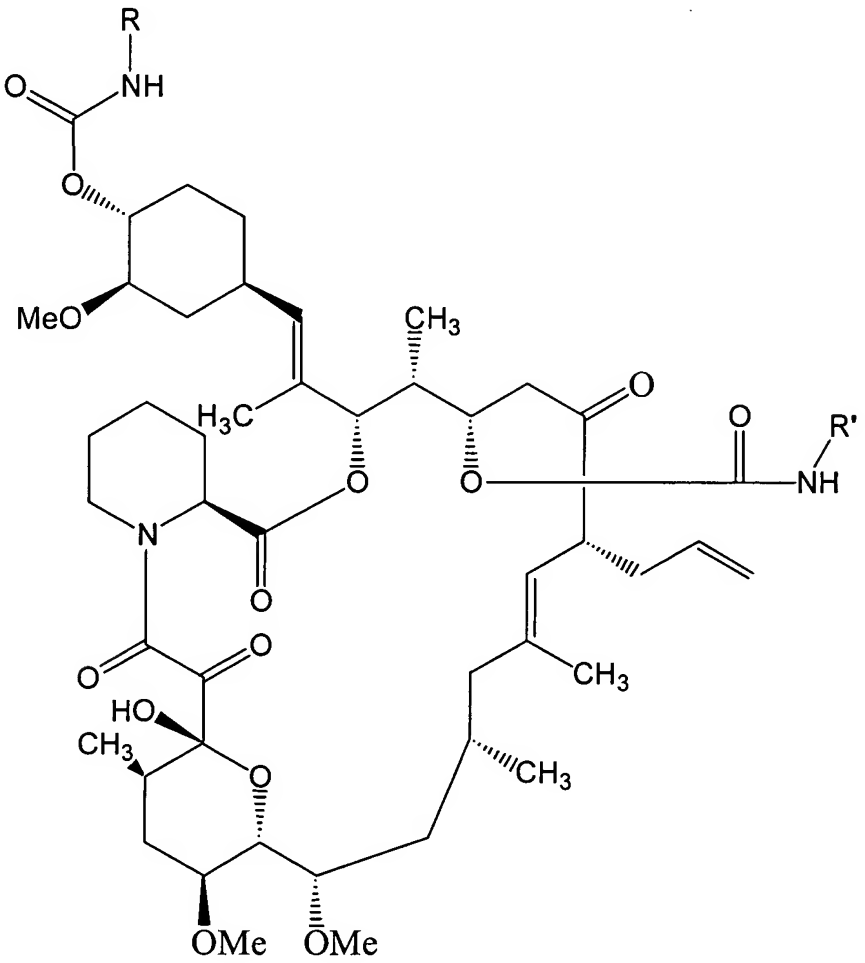
6 (amended) An assay releasing reagent for macrophilins comprising (a) an effective amount of the compound having the formula:



wherein R contains an alkyl, aryl, allyl, carbonyl, carboxylate, amide, ester, phosphonate, phosphate, sulfonate, sulfate, amidine, or carbamate functional group; and R" contains an alky aryl, allyl, carbonyl, carboxylate, amide, ester, phosphonate, phosphate, sulfonate, sulfate, amidine, or carbamate functional group or H; and

(b) a buffer solution.

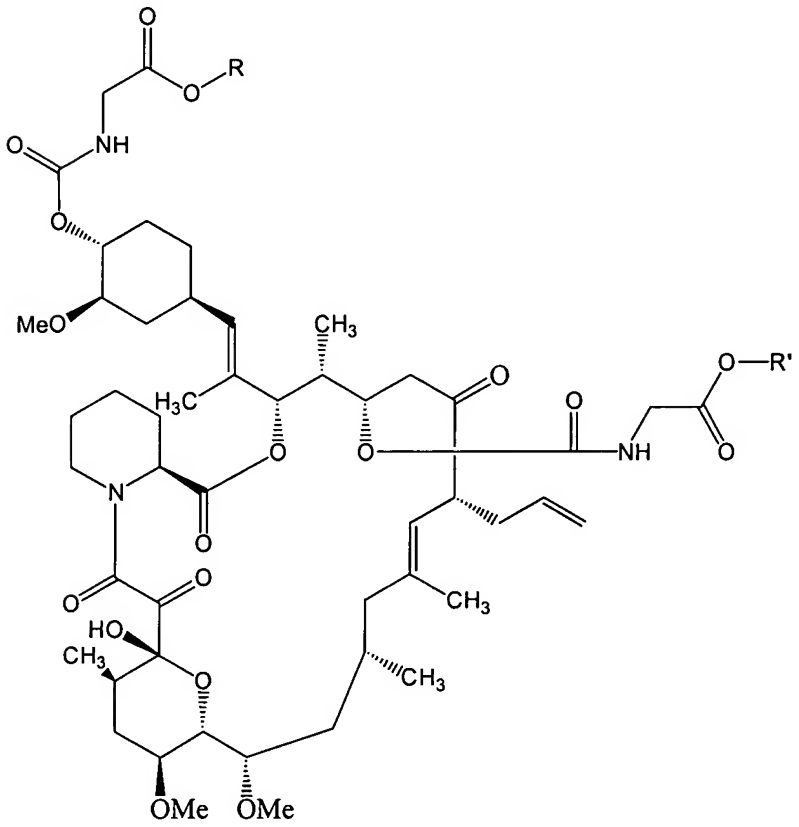
7 (amended) A method of determining the presence of a macrophilin-binding pharmaceutical in a sample comprising: adding a binding competitor of the formula:



wherein R is R is alkyl, aryl, allyl, each having less than 25 carbons or H, and
R' is alkyl, aryl, allyl, each having less than 25 carbons or H to the sample; adding a receptor that binds to the pharmaceutical but not significantly to the binding competitor; detecting the receptor-pharmaceutical and determining the amount of the pharmaceutical.

8 (originally presented) The method of claim 7 wherein the the pharmaceutical is rapamycin (sirolimus), everolimus or tacrolimus (FK506).

9 (amended) A method of determining the presence of a macrophilin-binding pharmaceutical in a sample comprising: adding a binding competitor of the formula:



wherein R is R is alkyl, aryl, allyl, each having less than 25 carbons or H, and
R' is alkyl, aryl, allyl, each having less than 25 carbons or H to the sample; adding a receptor that binds to the pharmaceutical but not significantly to the binding competitor; detecting the receptor-pharmaceutical and determining the amount of the pharmaceutical.

10 (originally presented) The method of claim 9 wherein the pharmaceutical is rapamycin (sirolimus), everolimus or tacrolimus (FK506).

11 (originally presented) The method of claim 10 wherein R or R' is ethyl.

12 (amended) A method of determining the presence of a macrophilin-binding pharmaceutical in a sample comprising: adding a binding competitor of the formula of claim 6 to the sample;

adding a receptor that binds to the pharmaceutical but not significantly to the binding competitor; detecting the receptor-pharmaceutical and determining the amount of the pharmaceutical.

13 (originally presented) The method of claim 12 wherein the pharmaceutical is rapamycin, (sirolimus), everolimus or tacrolimus (FK506).

14 (new) The method of claim 8 wherein R or R' is ethyl.